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APPLICATION NUMBER	FILING DATE	FIRST NAMED APPLICANT	ATTY. DOCKET NO.
09/383,916	08/26/99	ANDERSON	D 11712-792

EXAMINER

HM22/0227

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ART UNIT	PAPER NUMBER
GAMBEL, P 1644	9

DATE MAILED:

02/27/01

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

OFFICE ACTION SUMMARY

☑ Responsive to communication(s) filed on 12/8/00

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 D.C. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☑ Claim(s) 1, 16-20 is/are pending in the application.
Of the above, claim(s) 1, 20 is/are withdrawn from consideration.
☐ Claim(s) _____ is/are allowed.
☑ Claim(s) 16-19 is/are rejected.
☐ Claim(s) _____ is/are objected to.
☐ Claim(s) _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.
☐ The drawing(s) filed on _____ is/are objected to by the Examiner.
☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.
☐ The specification is objected to by the Examiner.
☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.
☐ received in Application No. (Series Code/Serial Number) _____.
☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☑ Notice of Reference Cited, PTO-892
☑ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____
☐ Interview Summary, PTO-413
☐ Notice of Draftperson's Patent Drawing Review, PTO-948
☐ Notice of Informal Patent Application, PTO-152

--SEE OFFICE ACTION ON THE FOLLOWING PAGES--

DETAILED ACTION

1. Applicant's election with traverse of Group II and the species psoriasis in Paper No. 8, filed 12/8/00, is acknowledged. The traversal is on the ground(s) that all of the species indicated fall under the scope of the generic claim. This is not found persuasive because of the reasons of record. Applicant should note the rejection under 35 USC, 112, first paragraph, set forth herein as well.

The species requirement is still deemed proper and is therefore made FINAL.

Claims 1 and 16-20 are pending.

Claims 2-15 have been canceled previously.

Claims 1 and 20 are withdrawn from further consideration by the examiner, 37 C.F.R. § 1.142(b) as being drawn to a nonelected invention/species.

2. Applicant should amend the first line of the specification to update the status of the priority documents. For example, USSN 08/487,550 is now U.S. Patent No. 6,113,898.

3. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed. Applicant should restrict the title to the claimed invention.

4. Formal drawings, filed 8/26/99, have been submitted which comply with 37 CAR 1.84.

5. The application is required to be reviewed and all spelling, TRADEMARKS, and like errors corrected. Trademarks should be capitalized or accompanied by the ™ or ® symbol wherever they appear and be accompanied by the generic terminology. Although the use of trademarks is permissible in patent applications, the proprietary nature of the trademarks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.
Appropriate corrections are required

6. The following is a quotation of the first paragraph of 35 U.S.C. § 112:
The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 16-19 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

In evaluating the facts of the instant case, the following is noted:

In vitro and animal model studies have not correlated well with in vivo clinical trial results in patients. Since the therapeutic indices of Immunosuppressive drugs such as costimulatory molecule-specific inhibitors can be species- and model-dependent, it is not clear that reliance on the experimental observations with the use of certain CD28:B7-specific inhibitors in certain in vitro and in vivo settings accurately reflects the relative efficacy of the claimed therapeutic strategy to treat any autoimmune condition with B7-specific antibodies. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Pharmaceutical therapies in the absence of in vivo clinical data are unpredictable for the following reasons; (1) the protein may be inactivated before producing an effect, i.e. such as proteolytic degradation, immunological inactivation or due to an inherently short half-life of the protein; (2) the protein may not reach the target area because, i.e. the protein may not be able to cross the mucosa or the protein may be adsorbed by fluids, cells and tissues where the protein has no effect; and (3) other functional properties, known or unknown, may make the protein unsuitable for in vivo therapeutic use, i.e. such as adverse side effects prohibitive to the use of such treatment. See page 1338, footnote 7 of Ex parte Aggarwal, 23 USPQ2d 1334 (PTO Bd. Pat App. & Inter. 1992).

Kahan clearly states that no in vitro immune assay predicts or correlates with in vivo immunosuppressive efficacy; there is no surrogate immune parameter as a basis of immunosuppressive efficacy and/or for dose extrapolation from in vitro systems to in vivo conditions (Cur. Opin. Immunol. 4: 553-560, 1992; see entire document, particularly page 558, column 2).

Blazar et al. (J. Immunol. 157: 3250-3259, 1996) disclose that anti-CD80 or anti-CD86 antibodies were ineffective in preventing T cell CD8-mediated GVHD lethality; that each antibodies was partially effective in CD4-mediated GVHD lethality and that the combination of anti-CD80 and anti-CD86 antibodies were effective in preventing GVHD lethality in murine experimental models (see entire document, including the Abstract)

Perrin et al. (J. Neuroimmunol. 65: 31-39,1996) disclose that in contrast to the effective treatment of disease with CTLA-4 Ig; anti-CD80 (B7-1) attenuated the first clinical disease episode but not the relapse, anti-CD86 (B7-2) had no significant effect on the course of disease, and the combined treatment with anti-CD80 plus anti-CD86 resulted in the exacerbation of disease (see entire document). It is also noted that CTLA-4 Ig had a marked but incomplete therapeutic effect in the EAE model.

In addition, Yi-qun et al. (Intl. Immunol. 8: 37-44, 1996) disclose that their findings have a number of important implications for therapeutic approaches (see entire document, particularly Discussion, last paragraph). It is clear that inhibition of T cell response to soluble antigens will require the blocking of both B7-2 and B7-1 to be effective. More, important it is unlikely that ongoing T cell response will be susceptible to inhibition by anti-B7 reagents, for example in autoimmune diseases.

Daikh et al. (J. Leukoc. Biol. 62: 156-162, 1997) disclose that the role of CD28-B7 interactions are complex in autoimmune diseases and that B7-1-specific antibodies can exacerbate disease in an experimental model of diabetes (see pages 159-160, Effects of Selective Blockade of B7-1 of B7-2 on Autoimmunity).

Immunosuppression and inhibition of immune disorders are much easier to achieve under controlled in vitro conditions that experienced in the human immunoregulatory diseases targeted by the claimed invention. Further, in animal models, the onset of inflammation is rapid with an aggressive destructive process, whereas in humans the disease progresses more slowly, often with natural periods of disease exacerbation and remission. Therefore, it should be noted that although the animal models validate concepts based on studies of human disease, such studies are generally limited to the "acute" as opposed to "chronic" nature of the disease. Furthermore, autoimmunity reflects a memory response or antigen-experienced immune response.

In view of the lack of predictability of the art to which the invention pertains the lack of established clinical protocols for effective costimulatory-based therapies, undue experimentation would be required to practice the claimed methods with a reasonable expectation of success, absent a specific and detailed description in applicant's specification of how to effectively practice the claimed methods and absent working examples providing evidence which is reasonably predictive that the claimed methods are effective for inhibiting any autoimmunity with B7-1-specific antibodies alone.

It is noted that treating psoriasis with B7-1-specific antibodies can be

7. Claims 17: It is apparent that the 16C10, 7C10, 20C9 and 7B6 antibodies are required to practice the claimed invention. As required elements, they must be known and readily available to the public or obtainable by a repeatable method set forth in the specification. If they are not so obtainable or available, the enablement requirements of 35 USC 112, first paragraph, may be satisfied by a deposit of the appropriate cell lines / hybridomas which produce these antibodies. See 37 CAR 1.801-1.809.

In addition to the conditions under the Budapest Treaty, applicant is required to satisfy that all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of a patent in U.S. patent applications.

Amendment of the specification to recite the date of deposit and the complete name and address of the depository is required. As an additional means for completing the record, applicant may submit a copy of the contract with the depository for deposit and maintenance of each deposit.

If the original deposit is made after the effective filing date of an application for patent, the applicant should promptly submit a verified statement from a person in a position to corroborate the fact, and should state, that the biological material which is deposited is a biological material specifically identified in the application as filed, except if the person is an attorney or agent registered to practice before the Office, in which the case the statement need not be verified. See MPEP 1.804(b).

It is noted that the sequence of an entire immunoglobulin satisfies the biological deposit of said immunoglobulin. Note that satisfaction for the biological deposit of the specific 16C10, 7C10, 20C9 and 7B6 antibodies require the disclosure and recitation of its entire amino acid sequences and not based upon partial sequences.

8. Claim 17 is rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 17 is indefinite in the recitation of "16C10, 7C10, 20C9 and 7B6" because their characteristics are not known. The use of "16C10, 7C10, 20C9 and 7B6" monoclonal antibodies as the sole means of identifying the claimed antibodies renders the claim indefinite because "16C10, 7C10, 20C9 and 7B6" are merely laboratory designations which do not clearly define the claimed products, since different laboratories may use the same laboratory designations to define completely distinct hybridomas / cell lines.

Applicant should specifically point out the support for any amendments made to the disclosure. See MPEP 714.02 and 2163.06

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371© of this title before the invention thereof by the applicant for patent.

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103© and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

11. Claims 16, 18-19 are rejected under 35 U.S.C. § 102(e) as being anticipated by Linsley et al. (U.S. Patent No. 5,885,579) (see entire document). Linsley et al. teach the use of B7-specific antibodies (columns 18-19, overlapping paragraph) to treat autoimmune diseases such as psoriasis (column 9, line 12) . Applicant is reminded that no more of the reference is required than that it sets forth the substance of the invention. The claimed functional limitations would be inherent properties of the referenced methods to treat psoriasis with B7:CD28-specific inhibitors such as B7-specific antibodies.

12. Claims 16 and 18-19 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Linsley et al. (U.S. Patent No. 5,885,579) in view of Nickoloff et al. (Blood 83: 2580-2586, 1994)

Linsley et al. teach the use of B7-specific antibodies to inhibit CD28-B7 interactions (columns 18-19, overlapping paragraph) in order to treat autoimmune diseases such as psoriasis (column 9, line 12) (see entire document). Linsley et al. Differ from the claimed methods by not exemplifying the treatment of psoriasis with B7-1-specific antibodies.

Nickoloff et al. teach the expression of B7-1 on lymphocytes in the chronic skin disorder of psoriasis, which, in turn, contributes to the ongoing T cell proliferation that occurs in the skin of patients afflicted by these disorders (see entire document, including the Discussion).

Given the clear teachings of Linsley et al. to use B7-specific antibodies to inhibit CD28-B7 interactions to treat an autoimmune disease such as psoriasis and given the teachings of Nickoloff et al. of the particular expression of B7-1 on T cells in the skin of psoriatic patients; the ordinary artisan would have been motivated to target B7-1 expressing cells in psoriasis. It would have been obvious to one of ordinary skill in the art to target B7-1-expressing cells with B7-1-specific antibodies alone or in combination with other immunosuppressives in order to inhibit in appropriate immune responses, including those associated with psoriasis. From the teachings of the references, it was apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

11. No claim is allowed.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phillip Gambel whose telephone number is (703) 308-3997. The examiner can normally be reached Monday through Thursday from 7:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

Phillip Gambel

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